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Term	Documents
LM609.USPT.	33
LM609S	0
TUMOR$	0
TUMOR.USPT.	31014
TUMORACTIVITY.USPT.	1
TUMORAL.USPT.	556
TUMORALALPHA.USPT.	1
TUMORALE.USPT.	3
TUMORALITY.USPT.	1
TUMORALLY.USPT.	24
(LM609 AND (TUMOR$ OR TUMOUR$ OR CANCER$ OR METASTASIS OR ANGIOGENESIS)).USPT.	33

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Refine Search: `lm609 and (tumor$ or tumour$ or cancer$ or metastasis or angiogenesis)` Clear

Search History

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USPT	lm609 and (tumor$ or tumour$ or cancer$ or metastasis or angiogenesis)	33	L1

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Logout

s s5 and lm609

```
            316  S5
            210  LM609
     S9       9  S5 AND LM609
? t s9/3/all
```

9/3/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12616539 BIOSIS NO.: 200000370041
Hypoxia induces differential expression of the integrin receptors alphavbeta3 and alphavbeta5 in cultured human endothelial cells.
AUTHOR: Walton Harry L; Corjay Martha H; Mohamed Seema N; Mousa Shaker A; Santomenna Linda D; Reilly Thomas M(a)
AUTHOR ADDRESS: (a)Cardiovascular Diseases Research, DuPont Pharmaceuticals Company, Wilmington, DE, 19880-0400**USA
JOURNAL: Journal of Cellular Biochemistry 78 (4):p674-680 12 June, 2000
MEDIUM: print
ISSN: 0730-2312
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

9/3/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11478112 BIOSIS NO.: 199800259444
Detection of tumor **angiogenesis** in vivo by alphavbeta3-targeted magnetic resonance imaging.
AUTHOR: Sipkins Dorothy A(a); Cheresh David A; Kazemi Mahmood R; Nevin Linda M; Bednarski Mark D; Li King C P
AUTHOR ADDRESS: (a)Lucas MRS Res. Cent., Dep. Radiol., Stanford Univ. Sch. Med., Stanford, CA 94305**USA
JOURNAL: Nature Medicine 4 (5):p623-626 May, 1998
ISSN: 1078-8956
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10930909 BIOSIS NO.: 199799552054
Immunohistochemical analysis of integrin **alpha-v-beta-3** expression on tumor-associated vessels of human carcinomas.
AUTHOR: Max Regina; Gerritsen Roland R C M; Nooijen Peet T G A; Goodman Simon L; Sutter Arne; Keilholz Ulrich; Ruiter Dirk J; De Waal Robert M W (a)
AUTHOR ADDRESS: (a)Dep. Pathol., Univ. Hosp. Nijmegen, P.O. Box 9101, 6500 HB Nijmegen**Netherlands
JOURNAL: International Journal of Cancer 71 (3):p320-324 1997

ISSN: 0020-7136
RECORD TYPE: Abstract
LANGUAGE: English

9/3/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2001 BIOSIS. All rts. reserv.

10064065 BIOSIS NO.: 199598518983
Antiintegrin **alpha-v-beta-3** blocks human breast cancer growth and **angiogenesis** in human skin.
AUTHOR: Brooks Peter C(a); Stromblad Staffan; Klemke Richard; Visscher Daniel; Sarkar Fazlul H; Cheresh David A
AUTHOR ADDRESS: (a)Dep. Immunol. Vascular Biol., Scripps Research Inst., 10666 North Torrey Pines Road, La Jolla, C**USA
JOURNAL: Journal of Clinical Investigation 96 (4):p1815-1822 1995
ISSN: 0021-9738
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2001 BIOSIS. All rts. reserv.

09948697 BIOSIS NO.: 199598403615
An antagonist of integrin **alpha-v-beta-3** prevents maturation of blood vessels during embryonic neovascularization.
AUTHOR: Drake Christopher J; Cheresh David A; Little Charles D(a)
AUTHOR ADDRESS: (a)Dep. Cell Biol., Cardiovascular Dev. Biol. Cent., Med. Univ. South Carolina, 171 Ashley Ave., Ch**USA
JOURNAL: Journal of Cell Science 108 (7):p2655-2661 1995
ISSN: 0021-9533
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2001 BIOSIS. All rts. reserv.

09795582 BIOSIS NO.: 199598250500
An antibody to the integrin **alpha-v-beta-3** inhibits ocular **angiogenesis**.
AUTHOR: Friedlander M; Shaffer R; Kincaid C; Brooks P; Cheresh D
AUTHOR ADDRESS: Dep. Cell Biology, Scripps Res. Inst., La Jolla, CA**USA
JOURNAL: Investigative Ophthalmology & Visual Science 36 (4):pS1047 1995
CONFERENCE/MEETING: Annual Meeting of the Investigative Ophthalmology and Visual Science Fort Lauderdale, Florida, USA May 14-19, 1995
ISSN: 0146-0404
RECORD TYPE: Citation
LANGUAGE: English

9/3/7 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2001 Elsevier Science B.V. All rts. reserv.

06873254 EMBASE No: 1997157582
Cytokine treatment of endothelial cells increases glycoprotein Ibalpha-dependent adhesion to von Willebrand factor
Beacham D.A.; Tran L.-P.; Shapiro S.S.

Dr. D.A. Beacham, Department of Medicine, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA 19107-5099 United States
Blood (BLOOD) (United States) 1997, 89/11 (4071-4077)
CODEN: BLOOA ISSN: 0006-4971
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 41

9/3/8 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10303207 20130051
Inhibition of corneal neovascularization by alpha(v)-integrin antagonists in the rat.
Klotz O; Park JK; Pleyer U; Hartmann C; Baatz H
Franz Volhard Clinic at Max Delbruck Center for Molecular Medicine, Campus Buch, University Hospital Charite, Berlin, Germany.
Graefe's archive for clinical and experimental ophthalmology (GERMANY) Jan 2000, 238 (1) p88-93, ISSN 0721-832X Journal Code: FPR
Languages: ENGLISH
Document type: JOURNAL ARTICLE

9/3/9 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10013874 99377072
Activation-dependent adhesion of human platelets to Cyr61 and Fisp12/mouse connective tissue growth factor is mediated through integrin alpha(IIb)beta(3).
Jedsadayanmata A; Chen CC; Kireeva ML; Lau LF; Lam SC
Department of Pharmacology, University of Illinois, Chicago, Illinois 60612, USA.
Journal of biological chemistry (UNITED STATES) Aug 20 1999, 274 (34) p24321-7, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: HL41793, HL, NHLBI; CA46565, CA, NCI; CA80080, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
? s s5 and review?

316 S5
2875350 REVIEW?
S10 13 S5 AND REVIEW?
? t s10/7/all

10/7/1 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

07902875 EMBASE No: 1999376368
Angiogenesis and arthritis
Walsh D.A.
D.A. Walsh, Rheumatology Acad. Univ. Nottingham, Clinical Sciences Building, City Hospital, Hucknall Road, Nottingham NG5 1PB United Kingdom
Rheumatology (RHEUMATOL.) (United Kingdom) 1999, 38/2 (103-112)
CODEN: RUMAF ISSN: 1462-0324
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 144

Indices of **angiogenesis** are increased in synovia from patients with arthritis, and vascular proliferation may contribute to the pathogenesis of synovitis, pannus growth, bone and cartilage destruction, and osteophyte formation. Pharmacological inhibition of **angiogenesis** therefore has potential as a therapeutic strategy in human arthritis. However, vascular growth is also essential for normal development, female reproduction and tissue repair. Selective inhibition of undesirable **angiogenesis** requires an understanding of the different regulatory mechanisms in pathological and physiological **angiogenesis**. This **review** outlines the evidence that the rate of **angiogenesis** is increased in the inflamed human synovium, and possible approaches to, and consequences of, the modulation of vascular growth.

10/7/2 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08555052 96418252
REVIEW: the integrin **alpha V beta 3**: **angiogenesis** and apoptosis.
Varner JA; Brooks PC; Cheresh DA
Department of Immunology, Scripps Research Institute, La Jolla, CA 92037, USA.
Cell adhesion and communication (SWITZERLAND) Nov 1995, 3 (4) p367-74, ISSN 1061-5385 Journal Code: B4A
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
(60 Refs.)

10/7/3 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

134176296 CA: 134(13)176296a JOURNAL
Integrin .alpha.v in health and disease - role of .alpha.v.beta.3 in metastasis, vascular remodeling and angiogenesis
AUTHOR(S): Mousa, Shaker A.; Varner, Judith A.; Cheresh, David
LOCATION: DuPont Pharmaceuticals Co., Wilmington, DE, USA
JOURNAL: Med. Intell. Unit DATE: 2000 VOLUME: 20 NUMBER: Angiogenesis Inhibitors and Stimulators PAGES: 37-44 CODEN: MIUNFS ISSN: 1080-3645
LANGUAGE: English PUBLISHER: R. G. Landes Co.
SECTION:
CA214000 Mammalian Pathological Biochemistry
IDENTIFIERS: review integrin alphav metastasis angiogenesis restenosis
DESCRIPTORS:
Integrins...
.alpha.v.beta.3; integrin .alpha.v.beta.3 and .alpha.v.beta.5 roles in metastasis, vascular remodeling and angiogenesis
Integrins...
.alpha.v.beta.5; integrin .alpha.v.beta.3 and .alpha.v.beta.5 roles in metastasis, vascular remodeling and angiogenesis
Angiogenesis... Apoptosis...
integrin .alpha.v.beta.3 and .alpha.v.beta.5 roles in metastasis, vascular remodeling and angiogenesis
Neoplasm...
metastasis; integrin .alpha.v.beta.3 and .alpha.v.beta.5 roles in metastasis, vascular remodeling and angiogenesis
Artery,disease...
restenosis; integrin .alpha.v.beta.3 and .alpha.v.beta.5 roles in metastasis, vascular remodeling and angiogenesis

10/7/4 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

133072048 CA: 133(6)72048j JOURNAL
Bone sialoprotein and the paradox of angiogenesis versus atherosclerosis
AUTHOR(S): Dong, Chunming; Goldschmidt-Clermont, Pascal J.
LOCATION: Heart and Lung Institute and Division of Cardiology, Department of Internal Medicine, College of Medicine and Public Health, Ohio State University, Columbus, OH, USA
JOURNAL: Circ. Res. DATE: 2000 VOLUME: 86 NUMBER: 8 PAGES: 827-828
CODEN: CIRUAL ISSN: 0009-7330 LANGUAGE: English PUBLISHER: Lippincott Williams & Wilkins
SECTION:
CA214000 Mammalian Pathological Biochemistry
CA202XXX Mammalian Hormones
IDENTIFIERS: review bone sialoprotein angiogenesis atherosclerosis
DESCRIPTORS:
Integrins...
.alpha.v.beta.1; bone sialoprotein as an angiogenic factor in assocn. with initiation of atherosclerosis in human
Integrins...
.alpha.v.beta.3; bone sialoprotein as an angiogenic factor in assocn. with initiation of atherosclerosis in human
Integrins...
.alpha.v.beta.5; bone sialoprotein as an angiogenic factor in assocn. with initiation of atherosclerosis in human
Angiogenesis... Atherosclerosis... Calcification... Cell adhesion... Cell migration... Cell proliferation... Osteocalcins... Osteonectin... Osteopontin... Sialoglycoproteins...
bone sialoprotein as an angiogenic factor in assocn. with initiation of atherosclerosis in human
Sialoglycoproteins...
BSP II (bone sialoglycoprotein II); bone sialoprotein as an angiogenic factor in assocn. with initiation of atherosclerosis in human
Blood vessel...
endothelium; bone sialoprotein as an angiogenic factor in assocn. with initiation of atherosclerosis in human
Blood vessel...
microvessel; bone sialoprotein as an angiogenic factor in assocn. with initiation of atherosclerosis in human
CAS REGISTRY NUMBERS:
106096-93-9 127464-60-2 bone sialoprotein as an angiogenic factor in assocn. with initiation of atherosclerosis in human

10/7/5 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

132033950 CA: 132(4)33950g JOURNAL
Role of integrins in cancer: survey of expression patterns (44435)
AUTHOR(S): Mizejewski, Gerald J.
LOCATION: Molecular Medicine, Wadsworth Center, New York State Department of Health, Albany, NY, 12201-0509, USA
JOURNAL: Proc. Soc. Exp. Biol. Med. DATE: 1999 VOLUME: 222 NUMBER: 2
PAGES: 124-138 CODEN: PSEBAA ISSN: 0037-9727 LANGUAGE: English
PUBLISHER: Blackwell Science, Inc.
SECTION:
CA214000 Mammalian Pathological Biochemistry
IDENTIFIERS: review integrin cancer
DESCRIPTORS:
Platelet(blood)...
aggregation; integrins in cancer
Actinins...

.alpha.-; integrins in cancer
Integrins...
.alpha.v.beta.1; integrins in cancer
Integrins...
.alpha.v.beta.3; integrins in cancer
Integrins...
.alpha.v.beta.5; integrins in cancer
Integrins...
.alpha.1.beta.1; integrins in cancer
Integrins...
.alpha.2.beta.1; integrins in cancer
Integrins...
.alpha.3.beta.1; integrins in cancer
Integrins...
.alpha.4.beta.1; integrins in cancer
Integrins...
.alpha.5.beta.1; integrins in cancer
Integrins...
.alpha.6.beta.1; integrins in cancer
Diagnosis...
cancer; integrins in cancer
Neoplasm...
diagnosis; integrins in cancer
CD antigens... Integrins...
integrin .alpha.7; integrins in cancer
Angiogenesis... Antitumor agents... Cell adhesion... Cell migration...
Cytoskeleton... Extracellular matrix... Integrins... Neoplasm... Prognosis
... Talin... Tumor markers... Vinculin...
integrins in cancer
Signal transduction,biological...
intercellular communication; integrins in cancer
Neoplasm...
metastasis; integrins in cancer
Mammary gland...
neoplasm; integrins in cancer
Cell aggregation...
platelet; integrins in cancer

10/7/6 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

131294990 CA: 131(22)294990h JOURNAL
Anti-integrins as a potential therapeutic target in angiogenesis
AUTHOR(S): Mousa, Shaker A.
LOCATION: DuPont Pharmaceuticals, Co., Wilmington, DE, 19880, USA
JOURNAL: Expert Opin. Ther. Pat. DATE: 1999 VOLUME: 9 NUMBER: 9
PAGES: 1237-1248 CODEN: EOTPEG ISSN: 1354-3776 LANGUAGE: English
PUBLISHER: Ashley Publications
SECTION:
CA201000 Pharmacology
IDENTIFIERS: review integrin angiogenesis inhibitor design, ECM protein
integrin angiogenesis inhibitor review
DESCRIPTORS:
Integrins...
.alpha.v.beta.3; anti-integrins as a potential therapeutic target in
angiogenesis
Integrins...
.alpha.v.beta.5; anti-integrins as a potential therapeutic target in
angiogenesis
Integrins...
.alpha.5.beta.1; anti-integrins as a potential therapeutic target in
angiogenesis
Angiogenesis inhibitors... Drug design...

anti-integrins as a potential therapeutic target in angiogenesis
Proteins,specific or class...
extracellular matrix-assocd.; anti-integrins as a potential therapeutic target in angiogenesis

10/7/7 (Item 5 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

131142646 CA: 131(11)142646n JOURNAL
Fibronectin and its integrin receptors in cancer
AUTHOR(S): Ruoslahti, Erkki
LOCATION: Cancer Research Center, The Burnham Institute, La Jolla, CA, 92037, USA
JOURNAL: Adv. Cancer Res. DATE: 1999 VOLUME: 76, PAGES: 1-20 CODEN: ACRSAJ ISSN: 0065-230X LANGUAGE: English PUBLISHER: Academic Press
SECTION:
CA214000 Mammalian Pathological Biochemistry
IDENTIFIERS: review fibronectin integrin neoplasm metastasis
DESCRIPTORS:
Integrins...
.alpha.IIb.beta.3; fibronectin and integrin receptors roles at several stages of tumor development and metastasis
Integrins...
.alpha.v.beta.3; fibronectin and integrin receptors roles at several stages of tumor development and metastasis
Integrins...
.alpha.v.beta.6; fibronectin and integrin receptors roles at several stages of tumor development and metastasis
Integrins...
.alpha.1.beta.1; fibronectin and integrin receptors roles at several stages of tumor development and metastasis
Integrins...
.alpha.5.beta.1; fibronectin and integrin receptors roles at several stages of tumor development and metastasis
Integrins...
.alpha.6.beta.4; fibronectin and integrin receptors roles at several stages of tumor development and metastasis
Angiogenesis... Cell adhesion... Cell migration... Fibronectins...
Integrins... Neoplasm...
fibronectin and integrin receptors roles at several stages of tumor development and metastasis
Neoplasm...
metastasis; fibronectin and integrin receptors roles at several stages of tumor development and metastasis
Phosphoproteins...
p125FAK; fibronectin and integrin receptors roles at several stages of tumor development and metastasis
Phosphoproteins...
SHC; fibronectin and integrin receptors roles at several stages of tumor development and metastasis
CAS REGISTRY NUMBERS:
144114-16-9 fibronectin and integrin receptors roles at several stages of tumor development and metastasis

10/7/8 (Item 6 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

131030681 CA: 131(3)30681p JOURNAL
The role of .alpha.v integrins during angiogenesis
AUTHOR(S): Eliceiri, Brian P.; Cheresh, David A.
LOCATION: Departments of Immunology and Vascular Biology, The Scripps

Research Institute, La Jolla, CA, 92037, USA
JOURNAL: Mol. Med. (N. Y.) DATE: 1998 VOLUME: 4 NUMBER: 12 PAGES: 741-750 CODEN: MOMEF3 ISSN: 1076-1551 LANGUAGE: English PUBLISHER: Springer-Verlag New York Inc.
SECTION:
CA215000 Immunochemistry
CA213XXX Mammalian Biochemistry
CA214XXX Mammalian Pathological Biochemistry
IDENTIFIERS: alphav integrin angiogenesis review
DESCRIPTORS:
Integrins...
.alpha.v.beta.3; .alpha.v integrins role during angiogenesis
Angiogenesis...
.alpha.v integrins role during angiogenesis
Integrins...
.alpha.v; .alpha.v integrins role during angiogenesis

10/7/9 (Item 7 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

130235438 CA: 130(18)235438r CONFERENCE PROCEEDING
Integrin .alpha.v in health and disease-role of .alpha.v.beta.3 in metastasis, vascular remodeling and angiogenesis
AUTHOR(S): Varner, Judith A.
LOCATION: Department of Medicine/Cancer Center, Cellular and Molecular Medicine, University of California, La Jolla, CA, USA
JOURNAL: Cell Adhes. Mol. Matrix Proteins EDITOR: Mousa, Shaker A (Ed),
DATE: 1998 PAGES: 71-84 CODEN: 67CWAV LANGUAGE: English PUBLISHER: Springer,Berlin, Germany
SECTION:
CA214000 Mammalian Pathological Biochemistry
IDENTIFIERS: review alphav integrin metastasis vascular remodeling angiogenesis
DESCRIPTORS:
Integrin .alpha.v... Integrins...
.alpha.v.beta.5; role of integrin .alpha.v.beta.3 in metastasis, vascular remodeling, and angiogenesis
Blood vessel...
remodeling; role of integrin .alpha.v.beta.3 in metastasis, vascular remodeling, and angiogenesis
Angiogenesis... Apoptosis... Arterial restenosis... Coronary artery restenosis... Integrin .alpha.v.beta.3... Melanoma... Metastasis(tumor)...
role of integrin .alpha.v.beta.3 in metastasis, vascular remodeling, and angiogenesis

10/7/10 (Item 8 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

128255388 CA: 128(21)255388m CONFERENCE PROCEEDING
The role of integrin .alpha.v.beta.3 in cell survival and angiogenesis
AUTHOR(S): Stromblad, Staffan; Brooks, Peter C.; Becker, Jurgen; Rosenfeld, Mauricio; Cheresh, David A.
LOCATION: Departments of Immunology and Vascular Biology, Scripps Research Institute, La Jolla, CA, 92037, USA
JOURNAL: Program. Cell Death, (Proc. Int. Symp.) EDITOR: Shi, Yun-bo (Ed), DATE: 1997 PAGES: 35-42 CODEN: 65SWAT LANGUAGE: English
MEETING DATE: 19960000 PUBLISHER: Plenum,New York, N. Y
SECTION:
CA213000 Mammalian Biochemistry
IDENTIFIERS: review integrin cell survival angiogenesis
DESCRIPTORS:

Angiogenesis... Apoptosis... Integrin .alpha.v.beta.3...
role of integrin .alpha.v.beta.3 in cell survival and angiogenesis

10/7/11 (Item 9 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

128060426 CA: 128(6)60426q JOURNAL
Integrin .alpha.v.beta.3: a therapeutic target
AUTHOR(S): Brooks, Peter C.
LOCATION: Dept. of Biochemistry, Norris Cancer Center, University of Southern California, Los Angeles, CA, 90033, USA
JOURNAL: Drug News Perspect. DATE: 1997 VOLUME: 10 NUMBER: 8 PAGES: 456-461 CODEN: DNPEED ISSN: 0214-0934 LANGUAGE: English PUBLISHER: J. R. Prous, S.A.
SECTION:
CA215000 Immunochemistry
IDENTIFIERS: review integrin alphaVbeta3 tumor angiogenesis
DESCRIPTORS:
Angiogenesis... Integrin .alpha.v.beta.3... Tumors(animal)...
integrin .alpha.v.beta.3 in tumor progression and angiogenesis is a therapeutic target

10/7/12 (Item 10 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

127229023 CA: 127(17)229023y JOURNAL
Stereoisomeric peptide libraries and peptidomimetics for designing selective inhibitors of the .alpha.v.beta.3 integrin for a new cancer therapy
AUTHOR(S): Haubner, Roland; Finsinger, Dirk; Kessler, Horst
LOCATION: Nuklearmedizinische Klinik Polyklinik, Technischen Universitat Munchen, Germany,
JOURNAL: Angew. Chem., Int. Ed. Engl. DATE: 1997 VOLUME: 36 NUMBER: 13/14 PAGES: 1374-1389 CODEN: ACIEAY ISSN: 0570-0833 LANGUAGE: English
PUBLISHER: Wiley-VCH
SECTION:
CA201000 Pharmacology
IDENTIFIERS: review antitumor integrin inhibitor peptide library
DESCRIPTORS:
Integrin .alpha.v.beta.3...
antagonists; stereoisomeric peptide libraries and peptidomimetics for designing selective inhibitors of the .alpha.v.beta.3 integrin for a new cancer therapy
Angiogenesis inhibitors... Drug design...
stereoisomeric peptide libraries and peptidomimetics for designing selective inhibitors of the .alpha.v.beta.3 integrin for a new cancer therapy
Peptide library...
stereoisomeric; stereoisomeric peptide libraries and peptidomimetics for designing selective inhibitors of the .alpha.v.beta.3 integrin for a new cancer therapy

10/7/13 (Item 11 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

124284943 CA: 124(21)284943m JOURNAL
The integrin .alpha.v.beta.3: angiogenesis and apoptosis
AUTHOR(S): Varner, Judith A.; Brooks, Peter C.; Cheresh, David A.
LOCATION: Department of Immunology, Scripps Research Institute, La Jolla,

CA, 92037, USA
JOURNAL: Cell Adhes. Commun. DATE: 1995 VOLUME: 3 NUMBER: 4 PAGES: 367-74 CODEN: CADCEF ISSN: 1061-5385 LANGUAGE: English
SECTION:
CA213000 Mammalian Biochemistry
IDENTIFIERS: review integrin angiogenesis apoptosis
DESCRIPTORS:
Blood vessel...
formation; integrin .alpha.v.beta.3 in angiogenesis and apoptosis
Apoptosis... Integrins,.alpha.v.beta.3...
integrin .alpha.v.beta.3 in angiogenesis and apoptosis

(Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12850011 BIOSIS NO.: 200100057160
Abciximab inhibits the migration and invasion potential of human coronary artery smooth muscle cells.
AUTHOR: Blindt Ruediger(a); Bosserhoff Anja-Katrin; Zeiffer Ute; Krott Nicole; Hanrath Peter; vom Dahl Juergen
AUTHOR ADDRESS: (a)Medical Clinic I, University Hospital, RWTH Aachen, Pauwelsstr 30, 52074, Aachen: ruediger.blindt@post.rwth-aachen.de** Germany
JOURNAL: Journal of Molecular and Cellular Cardiology 32 (12):p2195-2206 December, 2000
MEDIUM: print
ISSN: 0022-2828
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: In the EPIC trial, high-risk patients received the integrin receptor antagonist abciximab v placebo during and for 12 h following percutaneous coronary intervention with a significant 23% decrease of repeat revascularisation at 6 months. However, EPILOG and CAPTURE trials could not confirm these promising long-term results. Recently presented data from the EPISTENT trial suggested a beneficial effect of abciximab on restenosis in patients with diabetes. Based on these divergent results the aim of this study was to test whether alphavbeta3 receptor blockade by abciximab could cause inhibition of human coronary smooth muscle cell (hcSMC) proliferation, migration, and invasion which represent crucial steps during restenosis development. In contrast to quiescent hcSMCs, proliferating cells were capable to migrate towards chemoattractive stimuli and even capable to invade through a basement membrane equivalent. Abciximab and **LM609**, an alphavbeta3 specific **inhibiting** antibody, caused only a modest dose-dependent **inhibition** of hcSMC proliferation. On the contrary, the chemotactic and invasive potential of hcSMCs was significantly **inhibited** by abciximab administration 24 h prior to and during migration. (IC50 = 33.0 mug/ml for chemotaxis and IC50 = 0.5 mug/ml for invasion). For **LM609** similar results were obtained. Administration of the drugs just during migration without pretreatment **inhibited** migration equally but invasion to a lower extent (abciximab: IC50 = 32.6 mug/ml for chemotaxis and IC50 = 44.9 mug/ml for invasion; **LM609** IC50 = 3.1 mug/ml for chemotaxis and IC50 = 2.0 mug/ml for invasion). The attachment to the extracellular matrix proteins collagen I, collagen IV, laminin and vitronectin was not influenced. Pretreatment for 24 h with abciximab or **LM609** did not cause a downregulation of the alphavbeta3-integrin receptor. The results of this study indicate that the alphavbeta3 **antagonist** abciximab is a potent **inhibitor** of hcSMC migration and invasion which could explain the observed lower reintervention rate after PTCA and stent implantation.

3/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12828325 BIOSIS NO.: 200100035474
Inhibition of vascular smooth muscle cell adhesion and migration by c7E3 Fab (abciximab): A possible mechanism for influencing restenosis.
AUTHOR: Baron Julia H(a); Moiseeva Elena P; de Bono David P; Abrams Keith R ; Gershlick Anthony H
AUTHOR ADDRESS: (a)Division of Cardiology, Department of Medicine and Therapeutics, University of Leicester, Leicester**UK
JOURNAL: Cardiovascular Research 48 (3):p464-472 December, 2000
MEDIUM: print
ISSN: 0008-6363
DOCUMENT TYPE: Article
RECORD TYPE: Abstract

12828325 BIOSIS NO.: 200100035474
Inhibition of vascular smooth muscle cell adhesion and migration by c7E3 Fab (abciximab): A possible mechanism for influencing restenosis.
AUTHOR: Baron Julia H(a); Moiseeva Elena P; de Bono David P; Abrams Keith R ; Gershlick Anthony H
AUTHOR ADDRESS: (a)Division of Cardiology, Department of Medicine and Therapeutics, University of Leicester, Leicester**UK
JOURNAL: Cardiovascular Research 48 (3):p464-472 December, 2000
MEDIUM: print
ISSN: 0008-6363
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Objectives: Brief intravenous administration of chimeric antibody c7E3 Fab during coronary angioplasty has been shown in some studies to provide long term protection against coronary events. Smooth muscle cell (SMC) adhesion and migration are key initial steps in the development of restenosis. The purpose of this study was to investigate the effect of c7E3 Fab on adhesion and migration of SMC to the extracellular matrix (ECM) proteins osteopontin (Opn) and vitronectin (Vn). Methods: Adhesion of human vascular SMCs to ECM proteins was quantified using a CyQUANT assay kit. Migration of SMCs to Vh, Opn and PDGF was studied using a modified Boyden's chamber migration assay. Integrin expression was determined by immunoprecipitation. Results: c7E3 Fab reduced SMC adhesion on Vn and Opn to 69.2+-3.3% (P<0.001) and 52.5+-4.8% (P<0.001) respectively, compared to adhesion without antibody present. This reduction was the same as that for anti-alphavbeta3 integrin antibody LM609 (P=0.5). The combination of anti-alphavbeta5, integrin antibody and c7E3 Fab had a greater effect than either antibody alone (P<0.001). c7E3 Fab reduced SMC migration to Vn and Opn to 51.6+-8.9% (P<0.001) and 20.3+-6.1% (P<0.001) respectively, compared to migration in the absence of antibodies. Again, similar results were seen with **LM609**. PDGF-induced SMC migration was also **inhibited** by c7E3 Fab (P=0.004) and **LM609** (P=0.001), but to much less an extent. The migration SMCs from a culture found not to express the alphavbeta3 integrin was unaffected by these antibodies, strengthening the argument that c7E3 Fab inhibits SMC function via this integrin. Conclusions: c7E3 Fab inhibits the adhesion and migration of SMCs via the alphavbeta3 integrin. The inhibition, however, is partial, and varied depending on type of ECM protein and alphavbeta3 integrin expression. Some of the clinical benefits of c7E3 Fab may be due to its effect on SMCs.

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s (alphav(w)beta3 or alpha(w)v(w)beta(w)3) and angiogenesis

Processing
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            6077  BETA3
             101  ALPHAV(W)BETA3
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          850417  V
         1578874  BETA
         6018160  3
            2783  ALPHA(W)V(W)BETA(W)3
           39310  ANGIOGENESIS
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 6/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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08261961   BIOSIS NO.: 000043039234
MODULATION OF MICROVASCULAR ENDOTHELIAL CELL VNR GROWTH FACTORS AND GAMMA
  INTERFERON
AUTHOR: SWERLICK R A; LAWLEY T J; LI L J; CAUGHMAN S W; LEE K H; SEPP N T
AUTHOR ADDRESS: EMORY UNIV., ATLANTA, GA. 30322.
JOURNAL: KEYSTONE SYMPOSIUM ON INTEGRINS: CELL ADHESION AND TRANSMEMBRANE
COMMUNICATION IN DEVELOPMENT AND DISEASE, KEYSTONE, COLORADO, USA, APRIL
3-10, 1992. J CELL BIOCHEM SUPPL 0 (16 PART F). 1992. 180. 1992
CODEN: JCBSD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH


 6/7/2     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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07399406   93046914
  Thrombospondin as a mediator of cancer cell adhesion in metastasis.
  Walz DA
  Wayne State University School of Medicine, Department of Physiology,
Detroit, MI 48201.
  Cancer and metastasis reviews (UNITED STATES)   Nov 1992,  11 (3-4)
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p313-24, ISSN 0891-9992 Journal Code: C9H
Contract/Grant No.: HL 27073, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, ACADEMIC
Thrombospondin (TSP) is a 450 kDa adhesive glycoprotein. It is present in high concentrations in the platelet alpha-granule and can readily be secreted following platelet activation where local concentrations can be increased by 3-4 orders of magnitude. TSP is also synthesized by a variety of other cells and is incorporated into their extracellular matrix. TSP is a homotrimer with a number of functional domains, at least four of which might serve as receptor recognizing regions. The amino-terminal heparin binding domain interacts with heparin, other glycosaminoglycans and glycolipids and likely recognizes specific cell surface proteoglycans. The central disulfide cross-linked region, 210 kDa non-reduced and 70 kDa reduced, contains a peptide motif CSVTCG which is apparently responsible for binding to glycoprotein IV (CD36) with high affinity. Immediately adjacent to the calcium binding region of TSP, which undergoes considerable molecular relaxation in the absence of calcium, is an RGDA sequence. TSP has been demonstrated to bind to integrins of the **alpha v beta 3** and alpha IIb beta 3 class. The carboxy-terminal region of TSP also contains at least one binding epitope for a cell receptor. There are 2 well characterized genes for TSP and truncated forms of TSP have been detected which have inhibitory effects on **angiogenesis**. Finally, TSP can interact with fibrinogen and fibronectin, perhaps on cellular surfaces, which might serve as secondary receptor-like mechanisms for TSP binding and subsequent mediation of cell adhesion. (131 Refs.)

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? s s5 and py=1993

            316  S5
        1856109  PY=1993
     S7       3  S5 AND PY=1993
? t s7/7/all
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7/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09020568 BIOSIS NO.: 199497028938
Basic fibroblast growth factor modulates integrin expression in microvascular endothelial cells.
AUTHOR: Klein Sharon(a); Giancotti Filippo G; Presta Marco; Albelda Steven M; Buck Clayton A; Rifkin Daniel B
AUTHOR ADDRESS: (a)Dep. Cell Biol., New York Univ. Med. Cent., New York, NY 10016**USA
JOURNAL: Molecular Biology of the Cell 4 (10):p973-982 **1993**
ISSN: 1059-1524
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: During **angiogenesis** capillary endothelial cells undergo a coordinated set of modifications in their interactions with extracellular matrix components. In this study we have investigated the effect of the prototypical angiogenic factor basic fibroblast growth factor (bFGF) on the expression and function of several integrins in microvascular endothelial cells. Immunoprecipitation experiments with antibodies to individual subunits indicated that microvascular cells express at their surface several integrins. These include the alpha-1-beta-1, alpha-2-beta-1, and alpha-3-beta-1 laminin/collagen receptors; the alpha-6-beta-1 laminin receptor; the alpha-5-beta-1 and alpha-v-beta-1 fibronectin receptors; the alpha-6-beta-4 basement membrane receptor; and the **alpha-v-beta-3** and alpha-v-beta-5 vitronectin receptors. Treatment with bFGF caused a significant increase in the surface expression of the alpha-2-beta-1, alpha-3-beta-1, alpha-5-beta-1, alpha-6-beta-1, alpha-6-beta-4, and alpha-v-beta-5 integrins. In

contrast, the level of expression of the alpha-1-beta-1 and **alpha-v-beta-3** integrins was decreased in bFGF-treated cells. Immunoprecipitation of metabolically labeled cells indicated that bFGF increases the biosynthesis of the alpha-3, alpha-5, alpha-6, beta-4, and beta-5 subunits and decreases the production of the alpha-v and beta-3 subunits. These results suggest that bFGF modulates integrin expression by altering the biosynthesis of individual alpha or beta subunits. In accordance with the upregulation of several integrins observed in bFGF-treated cells, these cells adhered better to fibronectin, laminin, vitronectin, and type I collagen than did untreated cells. The largest differences in beta-1. integrin expression occurred apprx 72 h after exposure to bFGF, at a time when the expression of the endothelial cell-to-cell adhesion molecule endoCAM was also significantly upregulated. In contrast, a shorter exposure to bFGF (24-48 h) was required for the maximal induction of plasminogen activator production in the same cells. Taken together, these results show that bFGF causes significant changes in the level of expression and function of several integrins in microvascular endothelial cells.

7/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08982517 BIOSIS NO.: 199396134018
Endothelial cells adhere to the RGD domain and the fibrinogen-like terminal knob of tenascin.
AUTHOR: Joshi Paritosh; Chung Chang-Y; Aukhil Ikramuddin; Erickson Harold P (a)
AUTHOR ADDRESS: (a)Dep. Cell Biol., Duke Univ. Med. Cent., Durham, NC 27710 **USA
JOURNAL: Journal of Cell Science 106 (1):p389-400 **1993**
ISSN: 0021-9533
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have found that endothelial cells adhere much more strongly than fibroblasts to domains of tenascin and fibronectin. Endothelial cells adhered weakly, without spreading, to bacterial expression proteins corresponding to the tenth fibronectin type III (FN-III) domain of fibronectin, which contains the RGD. A larger fibronectin protein, containing this domain and the three amino-terminal 'synergy' domains gave strong adhesion and spreading. Two widely separated domains of tenascin gave adhesion. The third FN-III domain, TNfn3, which contains an RGD sequence in human and chicken tenascin, gave very strong adhesion and spreading of endothelial cells when tested as an isolated domain. Larger segments containing TNfn3 and the adjacent TNfn2 gave weaker adhesion, probably because the RGD sequence is partially blocked. Adhesion to this domain required divalent cations, was exquisitely sensitive to soluble GRGDSP peptide, and was blocked by antisera to the integrin **alpha-v-beta-3**. The second tenascin adhesion domain was the fibrinogen-like C-terminal knob, TNfbg. Cells adhered to but did not spread on this domain. This adhesion required divalent cations and was also sensitive to GRGDSP peptide, so it may be mediated by an integrin receptor. We have explored a range of conditions for preparing the adhesion substratum, and our results may resolve the controversy over whether tenascin can act as a substratum adhesion molecule. When coated for short times (1-2 hours) on plastic, tenascin had no adhesion activity, in contrast to fibronectin and the expression proteins, which gave strong adhesion under these conditions. When coated for longer times (12-24 hours) on plastic, the tenascin substratum supported good adhesion, but not spreading, of endothelial cells. Tenascin coated on nitrocellulose gave substantially stronger adhesion than on plastic, but still required long coating times for maximal activity. Adhesion of endothelial cells to native TN was inhibited by GRDGSP peptide. The cell

adhesion activity demonstrates the presence on endothelial cells of tenascin receptors, which may play a supportive role in **angiogenesis**, in the structure of blood vessels, or in binding tenascin to the cell surface to elicit or enhance a signalling function.

7/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08827884 BIOSIS NO.: 199395117235
Identification of a role of the vitronectin receptor and protein kinase C in the induction of endothelial cell vascular formation.
AUTHOR: Davis Cynthia M(a); Danehower Susan C; Laurenza Antonio; Molony J Leslie
AUTHOR ADDRESS: (a)Cell Biol. Dep., R and D 3.3244, Glaxo Inc. Res. Inst., 5 Moore Drive, Research Triangle Park, N**USA
JOURNAL: Journal of Cellular Biochemistry 51 (2):p206-218 **1993**
ISSN: 0730-2312
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: When cultured on a basement membrane substratum, endothelial cells undergo a rapid series of morphological and functional changes which result in the formation of histotypic tube-like structures, a process which mimics in vivo **angiogenesis**. Since this process is probably dependent on several cell adhesion and cell signaling phenomena, we examined the roles of integrins and protein kinase C in endothelial cell cord formation. Polyclonal antisera directed against the entire vitronectin (**alpha-v-beta-3**) and fibronectin (alpha-5-beta-1) receptors inhibited cord formation. Subunit-specific monoclonal antibodies to **alpha-v**, **beta-3**, and beta-1 integrin subunits inhibited cord formation, while monoclonal antibodies to alpha-5 did not, which implicated the vitronectin receptor, and not the fibronectin receptor, in vascular formation. Protein kinase C inhibitors inhibited cord formation, while phorbol 12-myristate 13-acetate (PMA) caused endothelial cells to form longer cords. Since the vitronectin receptor has been shown to be phosphorylated in an in vitro system by protein kinase C, the possible functional link between the vitronectin receptor and protein kinase C during cellular morphogenesis was examined. The vitronectin receptor was more highly phosphorylated in cord-forming endothelial cells on basement membrane than in monolayer cells on vitronectin. Furthermore, this phosphorylation was inhibited by protein kinase C inhibitors, and PMA was required to induce vitronectin receptor phosphorylation in endothelial cells cultured on vitronectin. Colocalization studies were also performed using antisera to the vitronectin receptor and antibodies to protein kinase C. Although no strict colocalization was found, protein kinase C was localized in the cytoskeleton of endothelial cells initially plated on basement membrane or on vitronectin, and it translocated to the plasma membrane of C-shaped cord-forming cells on basement membrane. Thus, both the vitronectin receptor and protein kinase C play a role in in vitro cord formation.

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? s s5 and py=1994

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? t s8/7/all
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8/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09640154 BIOSIS NO.: 199598095072

Integrin **alpha-v-beta-3** antagonists promote tumor regression by inducing apoptosis of angiogenic blood vessels..
AUTHOR: Brooks Peter C(a); Montgomery Anthony M P(a); Rosenfeld Mauricio(a); Reisfeld Ralph A(a); Hu Tianhua; Klier George; Cheresh David A(a)
AUTHOR ADDRESS: (a)Dep. Immunol., Scripps Research Inst., La Jolla, CA 92037**USA
JOURNAL: Cell 79 (7):p1157-1164 **1994**
ISSN: 0092-8674
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A single intravascular injection of a cyclic peptide or monoclonal antibody antagonist of integrin **alpha-v-beta-3** disrupts ongoing **angiogenesis** on the chick chorioallantoic membrane (CAM). This leads to the rapid regression of histologically distinct human tumors transplanted onto the CAM. Induction of **angiogenesis** by a tumor or cytokine promotes vascular cell entry into the cell apoptosis of the proliferative angiogenic vascular cells, leaving preexisting quiescent blood vessels unaffected. We demonstrate therefore that ligation of integrin **alpha-v-beta-3** is required for the survival and maturation of newly forming blood vessels, an event essential for the proliferation of tumors.

8/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09611134 BIOSIS NO.: 199598066052
Integrin **alpha-v-beta-3** differentially regulates adhesive and phagocytic functions of the fibronectin receptor alpha-4-beta-1.
AUTHOR: Blystone S D; Graham I L; Lindberg F P; Brown E J
AUTHOR ADDRESS: Dep. Med., Infect. Dis. Div., Washington Univ. Sch. Med., St. Louis, MO 63110**USA
JOURNAL: Molecular Biology of the Cell 5 (SUPPL.):p182A **1994**
CONFERENCE/MEETING: Thirty-fourth Annual Meeting of the American Society for Cell Biology San Francisco, California, USA December 10-14, 1994
ISSN: 1059-1524
RECORD TYPE: Citation
LANGUAGE: English

8/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09596654 BIOSIS NO.: 199598051572
Integrin **alpha-v-beta-3** differentially regulates adhesive and phagocytic functions of the fibronectin receptor alpha-5-beta-1.
AUTHOR: Blystone Scott D; Graham Irene L; Lindberg Frederik P; Brown Eric J (a)
AUTHOR ADDRESS: (a)Infectious Diseases, Campus Box 8051, Washington University Sch. Med., St. Louis, MO 63110**USA
JOURNAL: Journal of Cell Biology 127 (4):p1129-1137 **1994**
ISSN: 0021-9525
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The plasma protein fibronectin is an important opsonin in wound repair and host defense. To better understand the process of fibronectin-mediated phagocytosis, we have transfected K562 cells, which endogenously express alpha-5-beta-1, with **alpha-v-beta-**

3. In these transfectants, antibodies to **alpha-v-beta-3** block phagocytosis of fibronectin-opsonized beads completely, even though half the ingestion occurs through endogenous alpha-5-beta-1 receptors. alpha-5-beta-1-mediated adhesion to fibronectin-coated surfaces is unaffected by **alpha-v-beta-3** ligation. Neither alpha-v-beta-5 nor alpha-M-beta-2 ligation affects alpha-5-beta-1 phagocytic function in transfectants expressing these receptors. Pharmacologic data suggest that **alpha-v-beta-3** ligation suppresses the phagocytic competence of high affinity alpha-5-beta-1 receptors through a signal transduction pathway, perhaps involving protein kinase C. In addition to its significance for phagocytosis, **alpha-v-beta-3** regulation of alpha-5-beta-1 function may be significant for its roles in cell migration, metastasis, and **angiogenesis**.

8/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09483883 BIOSIS NO.: 199497492253
Basic fibroblast growth factor increases expression of the **alpha-v-beta-3** integrin complex on human microvascular endothelial cells.
AUTHOR: Sepp Norbert T; Li Lian-Jie; Lee Kwang H; Brown Eric J; Caughman S Wright; Lawley Thomas J; Swerlick Robert A(a)
AUTHOR ADDRESS: (a)Dep. Dermatol., WMB 5014, Emory Univ., Atlanta, GA 30322 **USA
JOURNAL: Journal of Investigative Dermatology 103 (3):p295-299 **1994**
ISSN: 0022-202X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Modulation of the expression of the **alpha-v-beta-3** complex on human dermal microvascular endothelial cells (HDMEC) may be crucial in wound healing and **angiogenesis**. Therefore, we examined the influence of basic fibroblast growth factor (bFGF), transforming growth factor beta, and interferon-gamma (IFN-gamma) on the expression of this complex. Stimulation of HDMEC with bFGF increased cell surface expression of both alpha-v and beta-3 in a dose- and time-dependent manner associated with the development of a spindled, elongated cell morphology. Northern blot analysis of HDMEC stimulated with bFGF demonstrated a marked increase in beta-3 but not alpha-v mRNA expression. Incubation of HDMEC with transforming growth factor-beta or interferon-y alone resulted in modest decreases in cell surface **alpha-v,beta-3**, and co-incubation of HDMEC with bFGF and transforming growth factor-beta or interferon-gamma inhibited bFGF-induced changes in cell morphology, increases in cell surface **alpha-v-beta-3** expression, and increases in beta-3 mRNA. These data demonstrate that both growth factors and proinflammatory cytokines alter the expression of **alpha-v-beta-3**, on microvascular endothelial cells and that these alterations correlate with changes in cell morphology.

8/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09257747 BIOSIS NO.: 199497266117
Requirement of vascular integrin **alpha-v-beta-3** for **angiogenesis**.
AUTHOR: Brooks Peter C; Clark Richard A F; Cheresh David A(a)
AUTHOR ADDRESS: (a)Dep. Immunol., Scripps Res. Inst., 10666 North Torrey Pines Road, La Jolla, CA 92037**USA

JOURNAL: Science (Washington D C) 264 (5158):p569-571 **1994**
ISSN: 0036-8075
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: **Angiogenesis** depends on the adhesive interactions of vascular cells. The adhesion receptor integrin **alpha-v-beta-3** was identified as a marker of angiogenic vascular tissue. Integrin **alpha-v-beta-3** was expressed on blood vessels in human wound granulation tissue but not in normal skin, and it showed a fourfold increase in expression during **angiogenesis** on the chick chorioallantoic membrane. In the latter assay, a monoclonal antibody to **alpha-v-beta-3** blocked **angiogenesis** induced by basic fibroblast growth factor, tumor necrosis factor-alpha, and human melanoma fragments but had no effect on preexisting vessels. These findings suggest that **alpha-v-beta-3** may be a useful therapeutic target for diseases characterized by neovascularization.

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L1: Entry 25 of 33 File: USPT Jul 29, 1997

US-PAT-NO: 5652109
DOCUMENT-IDENTIFIER: US 5652109 A
TITLE: Antibodies to .alpha.v.beta.3 integrin
DATE-ISSUED: July 29, 1997

US-CL-CURRENT: 435/7.1; 424/141.1, 424/143.1, 435/332, 435/334, 530/388.1

APPL-NO: 8/ 432542
DATE FILED: May 2, 1995

PARENT-CASE:
CROSS REFERENCES This application is a continuation of U.S. application Ser. No. 08/307,844 filed 30 Sep. 1994, which application is a 371 of PCT/US93/02987 filed Mar. 30, 1993, now U.S. Pat. No. 5,578,704 which application is a continuation in part of U.S. application Ser. No. 08/025,913 filed 3 Mar. 1993 (abandoned), which application is a continuation of U.S. application Ser. No. 07/862,679 filed 3 Apr. 1992 (abandoned), which applications are incorporated herein by reference and to which applications priority is claimed under 35 USC .sctn.120.

3/7/55 (Item 19 from file: 73)
DIALOG(R)File 73:EMBASE

04881743 EMBASE No: 1992021958
Recognition of osteopontin and related peptides by an alpha(v)betainf 3 integrin stimulates immediate cell signals in osteoclasts
Miyauchi A.; Alvarez J.; Greenfield E.M.; Teti A.; Grano M.; Colucci S.; Zambonin-Zallone A.; Ross F.P.; Teitelbaum S.L.; Cheresh D.; Hruska K.A.
Department of Medicine, Jewish Hosp Wash. Univ Med Ctr,St. Louis, MO 63110 United States
Journal of Biological Chemistry (J. BIOL. CHEM.) (United States) 1991 , 266/30 (20369-20374)
CODEN: JBCHA ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

We have investigated the nature of immediate cell signals produced by occupancy of the chicken osteoclast alpha(v)betainf 3 integrin. Synthetic osteopontin and peptides from the osteopontin and bone sialoprotein sequences containing Arg-Gly-Asp stimulated immediate reductions in osteoclast cytosolic Casup 2sup +. The changes in cytosolic Casup 2sup + required the Arg-Gly-Asp sequence and were blocked by a monoclonal antibody to the alpha(v)betainf 3 integrin, **LM609**. Osteoclast stimulation by the proteins through the integrin did not require immobilization since soluble peptides produced changes in cytosolic Casup 2sup + and **inhibited** osteoclast binding to bone particles and bone resorption. The decrease in cytosolic Casup 2sup + stimulated by osteopontin and related peptides appeared to be due to activation of a plasma membrane Casup 2sup +-ATPase by calmodulin. Thus, the data suggest that ligand binding to the osteoclast alpha(v)betainf 3 integrin results in calmodulin-dependent reduction in cytosolic Casup 2sup + which participates

07430756 BIOSIS NO.: 000091036745
THE VITRONECTIN RECEPTOR ALPHA-V-BETA-3 BINDS FIBRONECTIN AND ACTS IN CONCERT WITH ALPHA-5-BETA-1 IN PROMOTING CELLULAR ATTACHMENT AND SPREADING ON FIBRONECTIN
AUTHOR: CHARO I F; NANNIZZI L; SMITH J W; CHERESH D A
AUTHOR ADDRESS: COR THERAPEUTICS, INC., SOUTH SAN FRANCISCO, CALIF 94080.
JOURNAL: J CELL BIOL 111 (6 PART 1). 1990. 2795-2800. 1990
FULL JOURNAL NAME: Journal of Cell Biology
CODEN: JCLBA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The vitronectin receptor (.alpha.v.beta.3) is a member of the integrin superfamily of adhesive protein receptors that mediate a wide spectrum of adhesive cellular interactions, including attachment to vitronectin, von Willebrand factor, fibrinogen, and thrombospondin. We have studied the binding of fibronectin to the purified vitronectin receptor, and the role of this receptor in the attachment of cells to fibronectin. A solid-phase microtiter assay was developed to investigate the binding properties of the vitronectin receptor. Purified .alpha.v.beta.3 bound fibronectin with high affinity in a saturable, divalent cation-dependent manner. Binding was **inhibited** by soluble vitronectin, by RGD-containing peptides, and by **LM609**, a monoclonal antibody against the vitronectin receptor known to **inhibit** the binding of adhesive proteins to .alpha.v.beta.3. Immunoinhibition experiments showed that M21 humanmelanoma cells, which express the fibronectin receptor, .alpha.5.beta.1, as well as .alpha.v.beta.3, used both of these integrins to attach and spread on fibronectin. In support of this finding, M21-L cells, a varient cell line that specifically lacks .alpha.v.beta.3 but expresses .alpha.v.beta.1, attached and spread poorly on fibronectin. In addition, .alpha.v.beta.3 from surface-labeled M21 cells was retained, and selectively eluted by RGDS from a fibronectin affinity column. These rsults indicate that .alpha.v.beta.3 acts in concert with .alpha.5.beta.1 in promoting fibronectin recognition by these cells. We conclude that fibronectin binds to the .alpha.v.beta.3 vitronectin receptor specifically and with high affinity, and that this interaction is biologically relevant in supporting cell adhesion to

3/7/36 (Item 36 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05767873 BIOSIS NO.: 000084116280
HUMAN ENDOTHELIAL CELLS SYNTHESIZE AND EXPRESS AN ARG-GLY-ASP-DIRECTED ADHESION RECEPTOR INVOLVED IN ATTACHMENT TO FIBRINOGEN AND VON WILLEBRAND FACTOR
AUTHOR: CHERESH D A
AUTHOR ADDRESS: DEP. IMMUNOL., SCRIPPS CLINIC RES. FOUND., 10666 NORTH TORREY PINES ROAD, LA JOLLA, CALIF. 92037.
JOURNAL: PROC NATL ACAD SCI U S A 84 (18). 1987. 6471-6475. 1987
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Human umbilical vein endothelial cells express a heterodimeric adhesion receptor complex consisting of noncovalently associated .alpha. and .beta. subunits that under reducing conditions have molecular masses of 135 kDa and 115 kDa, respectively. This complex can be isolated in pure form from an affinity matrix consisting of an Arg-Asp-containing hepatapeptide and is specifically immunoprecipitated with monoclonal antibodies (mAbs) directed against the vitronectin receptor of human melanoma cells. These data suggest that this complex is one member of a large family of cell adhesion receptors. One of the mAbs, **LM609**, **inhibits** the attachment of human endothelial cells to fibrinogen, von Willebrand factor, and vitronectin yet has no effect on the attachment of these cells to fibronectin, collagen, or laminin. In addition, mAb **LM609 inhibits** attachment of endothelial cells to an immobilized synthetic peptide containing the Arg-Gly-Asp sequence. This adhesion receptor appears structurally similar to the IIb/IIIa glycoprotein complex expressed on platelets yet is antigenically distinct, since mAb LM609 fails to recognize IIb/IIIa glycoproteins. This receptor organizes in clusters on endothelial cells during their attachment to von Willebrand factor, vitronectin, or the Arg-Gly-Asp-containing heptapeptide. The data presented in this report suggest that Arg-Gly-Asp recognition may play a significant role in biological events associated with vascular proliferation.

07399126 93043313

Thrombospondin mediates adherence of CD36+ sickle reticulocytes to endothelial cells.

Sugihara K; Sugihara T; Mohandas N; Hebbel RP

Department of Medicine, University of Minnesota Medical School, Minneapolis.

Blood (UNITED STATES) Nov 15 1992, 80 (10) p2634-42, ISSN 0006-4971 Journal Code: A8G

Contract/Grant No.: HL30160, HL, NHLBI; HL31579, HL, NHLBI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Initiation of vasocclusion in sickle disease pathophysiology may involve abnormal red blood cell (RBC) adhesivity to endothelium, a phenomenon influenced by both RBC and plasma factors. Using human umbilical vein endothelial cells and a gravity sedimentation adherence assay, we have examined thrombospondin (TSP) as a plasma factor in this adhesive event. The already-abnormal adherence of sickle RBCs in buffer/albumin is significantly augmented ($P < .001$) by the addition of TSP, with half-maximal effect at about 0.3 microgram/mL. This effect is abolished by antibodies to either TSP or glycoprotein (GP) IV (CD36), as well as peptides RGDS and CSVTCG. The even greater adherence ($P < .005$) of sickle RBCs in autologous platelet-rich plasma (without added TSP) is dramatically **inhibited** by alpha CD36 antibodies (OKM5 and alpha GPIV) and significantly diminished by alpha TSP, by peptides RGDS and CSVTCG, and by two antibodies to the vitronectin receptor (7E3 and **LM609**). Studies of density-separated subpopulations and of RBC adhesion to immobilized proteins, as well as analysis of sickle RBCs using fluorescence-activated cell sorting and single cell microfluorometry, show that TSP responsiveness is a feature of the immature sickle "stress" reticulocytes, which carry CD36 (and not GPIIbIIIa-like receptors) as the TSP-receptive moiety. The endothelial cell's participation in this phenomenon appears to be more complex, and the data are consistent with the notion that it involves TSP interaction with other plasma proteins and/or multiple receptor structures. Other potential adhesogenic proteins (plasma von Willebrand factor, vitronectin, fibrinogen, and fibronectin) neither exhibited an affinity for reticulocytes nor supported increased sickle RBC adherence when added to buffer/albumin in these assay systems. In aggregate, our results indicate that TSP may be the major promoter of RBC adhesivity in plasma, and they suggest that therapeutic benefit might derive from interference with sickle reticulocyte CD36, as achieved by antibodies and CSVTCG in these studies.

08957750 BIOSIS NO.: 199396109251
Endothelial cell attachment and spreading on human tenascin is mediated by alpha-2-beta-1 and alpha-v-beta-3 integrins.
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ABSTRACT: Human umbilical vein endothelial cells were found to attach and partially spread on human tenascin. The attachment of endothelial cells to tenascin results in elongated cells with interconnecting processes and is distinct from the flattened appearance of endothelial cells on fibronectin, collagen, vitronectin or laminin substrata, suggesting a role for tenascin in modulating cell adhesion and motility. Endothelial attachment to tenascin was partially inhibitable by the SRRGDMS peptide derived from human tenascin and completely inhibitable by anti-integrin antibodies to alpha-2-beta-1 and alpha-V-beta-3. Endothelial cell attachment to tenascin could be inhibited up to 80% with anti-alpha-2 and anti-beta-1 monoclonal antibodies P1E6 and P4C10, respectively, and this was associated with a complete loss in cell spreading. In contrast. pretreatment of endothelial cells with the anti-alpha-V-beta-3 monoclonal antibody **LM609**, resulted in a 35% **inhibition** in cell attachment but did not alter cell spreading. In combination the anti-alpha-2 and anti-alpha-v-beta-3 antibodies, could completely abrogate cell spreading and attachment to tenascin-coated surfaces. Affinity purification of 125I labeled endothelial cell extract on a tenascin matrix column followed by immunoprecipitation with monoclonal antibodies to different integrin alpha and beta subunits resulted in the identification of alpha-2-beta-1 and alpha-2-beta-3 integrins, respectively, as tenascin binding receptors. Collagen affinity-purified alpha-v-beta-1 receptor from endothelial cells bound not only to collagen and laminin but also to tenascin in a radio receptor binding assay. The results demonstrate that alpha-2-beta-1 and alpha-V-beta-3 mediate distinct endothelial cell interactions with tenascin; cell spreading and cell binding, respectively. Binding by alpha-V-beta-3 is mediated by the SRRGDMS site on tenascin, whereas the alpha-2-beta-1 binding site remains undefined. The interaction of alpha-2-beta-1 and alpha-V-beta-3 with tenascin may be regulated in a cell type-specific manner as evidenced by the binding of endothelial cell alpha-2-beta-1 and alpha-V-beta-1 to tenascin, and the lack of binding by the same receptors on osteosarcoma

t s2/7/18,19,37,38,39

2/7/18 (Item 18 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09314935 BIOSIS NO.: 199497323305
Adhesive properties of osteopontin: Regulation by a naturally occurring thrombin-cleavage in close proximity to the GRGDS cell-binding domain.
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JOURNAL: Molecular Biology of the Cell 5 (5):p565-574 1994
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ABSTRACT: Osteopontin (OPN) is a secreted adhesive glycoprotein with a functional glycine-arginine-glycine-aspartate-serine (GRGDS) cell-binding domain. An interesting feature of OPN structure is the presence of a thrombin-cleavage site in close proximity to the GRGDS region. Cleavage of OPN by thrombin is likely to be of physiological importance, because cleavage of blood plasma OPN occurs naturally after activation of the blood coagulation pathway. To investigate functional consequences of OPN cleavage by thrombin, cell attachment and spreading assays were performed with uncleaved and cleaved forms of OPN. For all cell lines examined, thrombin-cleaved OPN promoted markedly greater cell attachment and spreading than uncleaved OPN. Cell attachment and spreading on thrombin-cleaved OPN was inhibited both by the soluble GRGDS peptides and an OPN-specific antibody raised to the GRGDS domain of OPN, thus implicating the GRGDS region in mediating the increased cell attachment and spreading observed on thrombin-cleaved OPN. Because the GRGDS sequence in OPN is only six residues from the thrombin-cleavage site, the data suggest the possibility that thrombin cleavage allows greater accessibility of the GRGDS domain to cell surface receptors. To investigate receptors that recognize uncleaved and thrombin-cleaved OPN, affinity chromatography was performed on placental extracts; the cell surface integrin alpha-v-beta-3 bound to columns constructed either with native or thrombin-cleaved OPN and was selectively eluted from each with soluble GRGDS peptide and EDTA. Moreover, adhesion assays performed in the presence of alpha-v-beta-3 blocking monoclonal antibody **LM609** identified alpha-v-beta-3 as a major functional receptor for thrombin-cleaved OPN. Several lines of evidence suggest that cleavage of OPN by thrombin occurs in vivo, such as in **tumors** and at sites of tissue injury, and adhesion assay data presented here indicate that such cleavage is important in the regulation of OPN function.

2/7/19 (Item 19 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08740047 BIOSIS NO.: 199395029398
Human melanoma cells derived from lymphatic metastases use integrin alpha-v-beta-3 to adhere to lymph node vitronectin.
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JOURNAL: Journal of Clinical Investigation 90 (4):p1406-1413 1992
ISSN: 0021-9738
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RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Human melanoma is a highly metastatic **cancer** and the regional lymph nodes are generally the first site of **metastasis**. Adhesion to cryostat sections of human lymph nodes was therefore studied using two human melanoma models established from lymph node metastases, namely, MeWo cell lines of diverse metastatic potentials and a highly metastatic cell line of recent origin designated MIM/8. We found a good correlation between the metastatic potentials of the melanoma cells as measured in nude mice and their ability to adhere to cryostat sections of human lymph nodes. When adhesion to immobilized extracellular matrix proteins was measured, a significant increase in adhesion, which correlated with increased **metastasis**, was seen mainly on vitronectin and to a lesser extent on fibronectin. The adhesion to vitronectin and to the frozen sections were specifically blocked by an RGD-containing peptide, mAb 661 to vitronectin and mAb **LM609** to integrin alpha-v-beta-3. FACS analysis revealed a significant and specific increase in cell surface expression of alpha-v-beta-3 on the metastatic cells as compared to the parent line. Together these results suggest that the adhesion of melanoma cells to lymph node vitronectin via the alpha-v-beta-3 receptor plays a role in the process of lymphatic dissemination.

2/7/37 (Item 17 from file: 73)
DIALOG(R)File 73:EMBASE

05490578 EMBASE No: 1993258677
Endothelial cell attachment and spreading on human tenascin is mediated by alphainf 2betainf 1 and alphavbetainf 3 integrins
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Journal of Cell Science (J. CELL SCI.) (United Kingdom) 1993, 105/4 (1001-1012)
CODEN: JNCSA ISSN: 0021-9533
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LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Human umbilical vein endothelial cells were found to attach and partially spread on human tenascin. The attachment of endothelial cells to tenascin results in elongated cells with interconnecting processes and is distinct from the flattened appearance of endothelial cells on fibronectin, collagen, vitronectin or laminin substrata, suggesting a role for tenascin in modulating cell adhesion and motility. Endothelial attachment to tenascin was partially inhibitable by the SRRGDMS peptide derived from human tenascin and completely inhibitable by anti-integrin antibodies to alphainf 2betainf 1 and alphavbetainf 3 Endothelial cell attachment to tenascin could be inhibited up to 80% with anti-alphainf 2 and anti-betainf 1 monoclonal antibodies P1E6 and P4C10, respectively, and this was associated with a complete loss in cell spreading. In contrast, pretreatment of endothelial cells with the anti-alphavbetainf 3 monoclonal antibody **LM609**, resulted in a 35% inhibition in cell attachment but did not alter cell spreading. In combination the anti-alphainf 2 and anti-alphavbetainf 3 antibodies, could completely abrogate cell spreading and attachment to tenascin-coated surfaces. Affinity purification of sup 1sup 2sup 5I-labeled endothelial cell ex-tract on a tenascin matrix column

followed by immunoprecipitation with monoclonal antibodies to different integrin alpha and beta subunits resulted in the identification of alphainf 2betainf 1 and alphavbetainf 3 integrins, respectively, as tenascin binding receptors. Collagen affinity-purified alphainf 2betainf 1 receptor from endothelial cells bound not only to collagen and laminin but also to tenascin in a radio receptor binding assay. The results demonstrate that alphainf 2betainf 1 and alphavbetainf 3 mediate distinct endothelial cell interactions with tenascin; cell spreading and cell binding, respectively. Binding by alphavbetainf 3 is mediated by the SRRGDMS site on tenascin, whereas the alphainf 2betainf 1 binding site remains undefined. The interaction of alphainf 2betainf 1 and alphavbetainf 3 with tenascin may be regulated in a cell type-specific manner as evidenced by the binding of endothelial cell alphainf 2beta1 and alphavbetainf 3 to tenascin, and the lack of binding by the same receptors on osteosarcoma MG63 to tenascin.

2/7/38 (Item 18 from file: 73)
DIALOG(R)File 73:EMBASE

05193905 EMBASE No: 1992334139
Human melanoma cells derived from lymphatic metastases use integrin alpha(v)betainf 3 to adhere to lymph node vitronectin
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Journal of Clinical Investigation (J. CLIN. INVEST.) (United States) 1992, 90/4 (1406-1413)
CODEN: JCINA ISSN: 0021-9738
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Human melanoma is a highly metastatic **cancer** and the regional lymph nodes are generally the first site of **metastasis**. Adhesion to cryostat sections of human lymph nodes was therefore studied using two human melanoma models established from lymph node metastases, namely, MeWo cell lines of diverse metastatic potentials and a highly metastatic cell line of recent origin designated MIM/8. We found a good correlation between the metastatic potentials of the melanoma cells as measured in nude mice and their ability to adhere to cryostat sections of human lymph nodes. When adhesion to immobilized extracellular matrix proteins was measured, a significant increase in adhesion, which correlated with increased **metastasis**, was seen mainly on vitronectin and to a lesser extent on fibronectin. The adhesion to vitronectin and to the frozen sections were specifically blocked by an RGD- containing peptide, mAb 661 to vitronectin and mAb **LM609** to integrin alpha(v)betainf 3. FACS(R) analysis revealed a significant and specific increase in cell surface expression of alpha(v)betainf 3 on the metastatic cells as compared to the parent line. Together these results suggest that the adhesion of melanoma cells to lymph node vitronectin via the alpha(v)betainf 3 receptor plays a role in the process of lymphatic dissemination.

2/7/39 (Item 19 from file: 73)
DIALOG(R)File 73:EMBASE

04524855 EMBASE No: 1991018897
The vitronectin receptor alpha(v)betainf 3 bind fibronectin and acts in concert with alpha$D5betainf 1 in promoting cellular attachment and spreading on fibronectin
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Journal of Cell Biology (J. CELL BIOL.) (United States) 1990, 111/6 I (2795-2800)

CODEN: JCLBA ISSN: 0021-9525
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The vitronectin receptor (alpha(v)betainf 3) is a member of the integrin superfamily of adhesive protein receptors that mediate a wide spectrum of adhesive cellular interactions, including attachment to vitronectin, von Willebrand factor, fibrinogen, and thrombospondin. We have studied the binding of fibronectin to the purified receptor, and the role of this receptor in the attachment of cells to fibronectin. A solid-phase microtiter assay was developed to investigate the binding properties of the vitronectin receptor. Purified alpha(v)betainf 3 bound fibronectin with high affinity in a saturable, divalent cation-dependent manner. Binding was inhibited by soluble vitronectin, by RGD-containing peptides, and by **LM609**, a monoclonal antibody against the vitronectin receptor known to inhibit the binding of adhesive proteins to alpha(v) betainf 3. Immunoinhibition experiments showed that M21 human melanoma cells, which express the fibronectin receptor, alpha$D5betainf 1, as well as alpha(v)betainf 3, used both of these integrins to attach and spread on fibronectin. In support of this finding, M21-L cells, a variant cell line that specifically lacks alpha(v)betainf 3 but expresses alpha(v)beta sup 1, attached and spread poorly on fibronectin. In addition, alpha(v)betainf 3 from surface-labeled M21 cells was retained, and selectively eluted by RGDS from a fibronectin affinity column. These results indicate that alpha(v)betainf 3 acts in concert with alpha$D5betainf 1 in promoting fibronectin recognition by these cells. We conclude that fibronectin binds to the alpha(v)betainf 3 vitronectin receptor specifically and with high affinity, and that this interaction is biologically relevant in supporting cell adhesion to matrix proteins.